UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,464	11/07/2005	Daphna J Havkin-Krenkel	RUCC-0064	1631

23973 7590 10/28/2008

DRINKER BIDDLE & REATH
ATTN: INTELLECTUAL PROPERTY GROUP
ONE LOGAN SQUARE
18TH AND CHERRY STREETS
PHILADELPHIA, PA 19103-6996

EXAMINER	
FRONDA, CHRISTIAN L	
ART UNIT	PAPER NUMBER
1652	

MAIL DATE	DELIVERY MODE
10/28/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,464	HAVKIN-KRENKEL ET AL.	
	Examiner	Art Unit	
	CHRISTIAN L. FRONDA	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 October 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *15-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 April 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/7/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group I (claims 1-14) in the reply filed on 10/10/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 15-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention. The requirement is still deemed proper and is therefore made FINAL.

2. Claims 1-14 are under consideration in this Office Action.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants are directed toward the current USPTO Written Description Training Materials made available to the public on 04/11/2008 for information regarding examination of patent claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph.

The claims are genus claims encompassing transgenic organisms comprising expressible transgenes encoding a genus of 3-O-methyltransferases for which no sequence and structure is apparent and a genus of chain-shortening enzymes for which no sequence and structure is apparent.

The scope of each genus includes many members with widely differing amino acid sequences and structures, where each genus is highly variable because a significant number of structural and biological differences between genus members exists.

While the specification discloses an isolated *E. coli* host cell transformed with a polynucleotide of SEQ ID NO: 1 encoding the *Vanilla planifolia* 3-O-methyltransferase of SEQ ID NO: 2; the specification, however, does not describe and define any structural features, nucleotide/amino acid sequences, and/or biological functions that are commonly possessed by members of each genus. The specification dos not provide a correlation between any structure, other than SEQ ID NO: 2, and the activity of catalyzing methylation of caffeic acid to ferulic acid based on which those of ordinary skill in the art could predict the structure and amino acid sequence of any enzyme that catalyzes the methylation of caffeic acid to ferulic acid. Further, there is no art-recognized correlation between any structure, other than SEQ ID NO: 2, and the activity of catalyzing methylation of caffeic acid to ferulic acid based on which those of ordinary skill in the art could predict the structure and amino acid sequence of any enzyme that catalyzes the methylation of caffeic acid to ferulic acid.

MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification fails to disclose additional 3-O-methyltransferases chain-shortening enzymes. As such the disclosure of the above mentioned polynucleotide of SEQ ID NO: 1 encoding the *Vanilla planifolia* 3-O-methyltransferase of SEQ ID NO: 2 is insufficient to be representative of the attributes and features common to all the members of each claimed genus.

Vas-Cath, Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry,

whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class, where the specification provided only the bovine sequence.

In view of the above considerations, one of skill in the art would not recognize that applicants were in possession of the each claimed genus.

Regarding the recited "transgenes", gene elements which are not particularly described by the specification including untranslated regions and regulatory elements such as promoter, repressor, inducer, and enhancer elements are essential to the function of the invention since the claims encompass genes encoding the recited 3-O-methyltransferase and chain-shortening enzyme. The structure of these untranslated regions and regulatory elements which applicants considers as being essential to the function of the claim are unpredictable and not conventional in the art; and therefore, these untranslated regions and regulatory elements must be empirically determined. Although the specification discloses the nucleotide sequence of SEQ ID NO: 1, there is no known or disclosed correlation between the coding region of a polynucleotide and the structure of the non-described regulatory elements, such as promoter, repressor, inducer, and enhancer The specification does not provide a complete and detailed description for untranslated regions and regulatory elements of the claimed "transgenes".

According to MPEP 2163 II. METHODOLOGY FOR DETERMINING ADEQUACY OF WRITTEN DESCRIP-TION:

> "…disclosure of a partial structure without additional characterization of the product may not be sufficient to evidence possession of the claimed invention. See, e.g., *Amgen*, 927 F.2d at 1206, 18 USPQ2d at 1021 ("A gene is a chemical compound, albeit a complex one, and it is well established in our law that conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials, and to describe how to obtain it. Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by its principal biological property, e.g., encoding

> human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated.")"

Therefore, in view of the above considerations one of skill in the art would not recognize that applicants were in possession of the claimed "transgenes".

5. Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated microorganism host cell transformed with a polynucleotide of SEQ ID NO: 1 encoding the *Vanilla planifolia* 3-O-methyltransferase of SEQ ID NO: 2; **does not** reasonably provide enablement for any transgenic organism as recited comprising any expressible transgenes encoding any 3-O-methyltransferase for which no sequence and structure is apparent and any chain-shortening enzyme for which no sequence and structure is apparent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

According to MPEP 2164.01(a), factors considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

MPEP§ 2164.04 states that while the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification

fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. Accordingly, the factors most relevant to the instant rejection are addressed in detail below.

The nature and breadth of the claims encompass any transgenic organism as recited comprising any expressible transgenes encoding any 3-O-methyltransferase for which no sequence and structure is apparent and any chain-shortening enzyme for which no sequence and structure is apparent.

The reference of Chica et al. (Curr Opin Biotechnol. 2005 Aug;16(4):378-84; PTO 892) teaches that the complexity of the structure/function relationship in enzymes has proven to be the factor limiting the general application of rational enzyme modification and design, where rational enzyme modification and design requires in-depth understanding of structure/function relationships.

In regard to making transgenic animals, the unpredictability of the art is very high. For example, Wang et al. (Nuc. Acids Res. 27: 4609-4618, 1999; pg 4617; PTO 892) surveyed gene expression in transgenic animals and found in each experimental animal with a single "knock-in" gene, multiple changes in genes and protein products, often many of which were unrelated to the original gene. Likewise, Kaufman et al (Blood 94: 3178-3184, 1999; PTO 892) found transgene expression levels in their transfected animals varied from "full" (9 %) to "intermediate" to "none" due to factors such as "vector poisoning" and spontaneous structural rearrangements (pg 3180, col 1, 2nd full paragraph; pg 3182-3183).

The specification provides guidance, prediction, and working examples for an isolated *E. coli* host cell transformed with a polynucleotide of SEQ ID NO: 1 encoding the *Vanilla planifolia* 3-O-methyltransferase of SEQ ID NO: 2. However, the specification does not provide guidance, prediction, and working examples for making and/or using the invention as claimed.

The specification dos not provide a correlation between any structure, other than SEQ ID NO: 2, and the activity of catalyzing methylation of caffeic acid to ferulic acid based on which those of ordinary skill in the art could predict the structure and amino acid sequence of any enzyme that catalyzes the methylation of caffeic acid to ferulic acid. Further, there is no art-recognized correlation between any structure, other than SEQ ID NO: 2, and the activity of

catalyzing methylation of caffeic acid to ferulic acid based on which those of ordinary skill in the art could predict the structure and amino acid sequence of any enzyme that catalyzes the methylation of caffeic acid to ferulic acid.

Thus, one must perform an enormous amount of trial and error experimentation to search and screen for the 3-O-methyltransferase and the chain-shortening enzyme from any biological source, transforming an organism with the nucleic acids encoding the enzymes, and then determining whether the transgenic organism can produce vanillin when provided with caffeic acid or an esterified derivative thereof.

Therefore, in view of the overly broad scope of the claims, the specification's lack of specific guidance and prediction, the specification's lack of additional working examples, and the amount of experimentation required; it would require undue experimentation for a skilled artisan to make and use the claimed invention. Without sufficient guidance, the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue. See *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988).

Conclusion

6. No claims are allowed.

7. The following reference made of record and not relied upon is considered pertinent to applicant's disclosure: Wein et al. (Plant J. 2002 Sep;31(6):755-65; PTO 892) teach isolation, cloning and expression of a multifunctional O-methyltransferase from strawberry capable of forming 2,5-dimethyl-4-methoxy-3(2H)-furanone (see entire publication).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christian L Fronda whose telephone number is (571)272-0929. The examiner can normally be reached Monday-Thursday and alternate Fridays between 9:00AM - 5:00PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on (571)272-0934. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

9. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Christian L. Fronda/
Primary Examiner
Art Unit 1652